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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,598	11/25/2005	Anders Pettersson	059490-5042-US	3677

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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
YOUNG, MICAH PAUL	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,598	PETTERSSON ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38,41,42 and 44-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38,41,42 and 44-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknoweldgment of Papers Received: Amendment/Response dated 10/29/07

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-38, 41, 42, 44, 50, 51, 53-70, 73-77 and 79-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saslawski et al (WO 99/33448 hereafter '448) in view of ***H. Hedenstrom*** et al (*Intragastric pH after...*; Ailment Pharmacol Ther, 1997; 11:1137-1141). The claims are drawn to a dosage from comprising a proton pump inhibitor and an H2 receptor antagonist where the active agents have different release rates. The claims further recite methods of making the dosage form.

4. The '448 patent discloses a multi-layered formulation comprising multiple active agents such as ranitidine, famotidine and omeprazole (page 7, line 10-15). The drugs are present in

separate layers where the first outer layer provides an immediate release and the second inner layer provides a prolonged sustained release of the active agent (abstract). The inner layer can be in the form of a core while the outer layer is a matrix in which the second drug is dispersed (abstract). The layers comprise excipients such as methacrylate copolymers, magnesium oxide, calcium phosphate, alginates, hydrogenated vegetable oils, and various common excipients (page 9, line 18-page 10, line 35). The tablets formed can be further coated with an enteric polymer (page 15, line 3-12). The dosage form can be effervescent comprising sodium bicarbonate (page 9, lin. 31-38). The formulation comprising multiple granules that are essentially mixtures of excipients, an active agent and disintegrants suitable for the release. The method for making the tablet comprises preparing a first granulation comprising a first active agent and associated polymers and excipients, followed by preparing a second granulation with a different agent. The granulations are combined in a manner to crate a compressed tablet with a first immediate release layer and a second controlled release layer (page 15, line 12-page 16, lin. 20). In cases of a core structure the second outer layer is applied by compression in a chamber (page 18, lin. 1-15). The resulting formulation dissolves in gastric juices (examples).

5. Regarding the claims which recite the limitation that the dosage from is capable of raising the gastric pH above 4, it is the position of the Examiner that such a limitation would be inherently met by the formulation of the since the dosage forms comprise high doses of active agents including proton pump inhibitors. This is evidenced by the ***Hedenstrom*** study, which discloses 2 hours after administration the gastric pH had risen above 4 for dosages of ranitidine and famotidine (figure 1). Any composition comprising at least the amounts of the compounds would also raise the gastric pH. The dosage forms were each fast acting easily administered.

From this study a skilled artisan would see that fats acting H2 receptor agonists would inherently raise the gastric pH above 4 within 2 hours of administration.

6. The reference discloses multiple drugs for the formulation including those of the instant claims. The reference however does not exemplify those compounds as explicitly separated into immediate release and delayed release layers. The reference further is silent to the specific concentrations of the alginate or individual compounds. The examples show a high dosage of each compound from ~225 mg-600mg (examples). The formulation comprises disintegrants like sodium alginate, and is present in the formulation in concentration of ~2-15% by weight of the immediate release layer. This is ~50-80 mg of disintegrant present in the formulation (examples). These disclosures meet the general conditions of the claims. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

7. Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various pharmaceutical compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

8. With these aspects in mind it would have been obvious to follow the suggestions and teachings of the '448 patent in order to produce a stable tablet for instant and prolonged release of compounds useful in treating GERD as described in the ***Hedenstrom***. The formulation could

be effervescent with the inclusion of the alkali compound and become dispersed in water for deliver. One of ordinary skill in the art would have been motivated to follow these teachings and suggestions with an expected result of a stable biphasic release tablet.

9. Claims 1, 40, 42, 45-48, 52, 71, 73 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saslawski et al (WO 99/33448 hereafter '448) in view of ***H. Hedenstrom*** et al (*Intragastric pH after...*; Ailment Pharmacol Ther, 1997; 11:1137-1141) and ***M. Gschwantler*** et al (*Famotidine verses omeprazole ...*; Ailment Pharmacol Ther, 1999; 13:1063-1069). The claims are drawn to a method of treating a bacterial infection with a formulation comprising H2 receptor agonists and proton pump inhibitors.

10. As discussed above the '448 patent discloses a formulation comprising multiple compounds including both H2 receptor agonist and proton pump inhibitors in separate layers with differing release profiles. Also discussed above, these formulations would inherently raise the gastric pH of an individual upon administration due to the nature of the H2 receptor agonist present in the formulation. It would also be equally inherent to use the formulation of the prior art to eradicate a bacterial infection as evidenced by the ***M. Gschwantler*** study. The study discloses that famotidine regimens were successful in eradicating *H. pylori* infections (abstract). The study was a long-term study over several weeks. The results showed a low dose of famotidine was sufficient to completely eradicate a clarithromycin resistant strain of bacterial infection. An artisan would have been motivated to apply the formulation of the '448 in a long-term eradication therapy that simultaneously also treat symptoms of GERD since the compound inherently posses these properties

11. With these aspects in mind it would have been obvious follow the suggestions and teachings of the '448 patent in order to produce tablets useful in treating bacterial infections and GERD symptoms. One of ordinary skill in the art would have been motivated to follow these suggestions with an expected result of a stable tablet capable of eradicating a bacterial infection and treating symptoms of GERD.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 30-38,41,42 and 44-86 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 49-110 of copending Application No. 11/544,750. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of treating

a patient with a dosage form comprising a proton pump inhibitor and an H2 receptor antagonist, where the conditions include GERD and other gastro-intestinal disorders.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

14. Applicant's arguments filed 10/29/07 have been fully considered but they are not persuasive. Applicant argues that:

a. At the time of the invention there would have been no motivation to combine an H2 receptor antagonist with a proton pump inhibitor

b. The '448 patent does not obviate the instant invention since the two active agents are the ***same*** active ingredient, and therefor would not provide a composition combining an H2 receptor antagonist and a proton pump inhibitor.

15. Regarding arguments a. and b., it remains the position of the Examiner that the combination of the '448 patent with the ***H. Hedenstrom*** and ***M. Gschwantler*** studies provides methods for treating various infections and or gastro-intestinal disorders. Firstly the '448 patent teaches a bilayered dosage form comprising the prolonged release and immediate release of two separate active agents. Included in these active agents include proton pump inhibitors such as omeprazole and H2 receptor agonists such as cimetidine, ranitidine and famotidine (page 7, lin. 10-12). The dosage from comprises disintegrants, and other excipients useful in the controlled release of the dosage form. The dosage form of the '448 patent discloses each of the physical parameters of the instant claims. The patent establishes the functional equivalency of

omeprazole, ranitidine, famotidine and nizatidine, while the ***H. Hedenstrom*** study establishes that these compounds are useful for treating the same symptoms in different ways. The study establishes that omeprazole should be released over an extended period of time for best long term effects, while the ranitidine and famotidine can be released immediately for best effects. Also the study established that the slow acting omeprazole should be combined with another more immediately acting compound in order to treat to effect (treat immediate symptoms as they arise). Taken together it would have been obvious at the time of the invention to provides a combined dosage from to treat immediate symptoms of GERD and provide for prolonged disorder treatment. Applicant argues that the '448 patent teaches away from the instant invention by disclosing an embodiment where both active agents are the same. However Applicant is directed to the proceeding paragraph where the patent clearly discloses that the first and second may contain a different active ingredient (page 4, lin. 12-14). This disclosure taken with the further teachings of the patent (the excipients and specific active agents to combined and released) along with the teachings of the ***H. Hedenstrom*** study it remains the position of the Examiner that the combination obviates the claims.

16. Regarding the combination of the '448 patent, ***H. Hedenstrom*** and ***M. Gschwantler*** studies, it remains the position of the Examiner that such a combination would obviate the method of the instant claims. As discussed above the combination of the '448 patent with the ***H. Hedenstrom*** provides a dosage from comprising an H2 receptor antagonist and a proton pump inhibitor in a controlled release formulation along with a method of treat with various gastro-intestinal disorders. The ***M. Gschwantler*** study establishes that famotidine regimens were successful in eradicating *H. pylori* infections. Famotidine as disclosed by the ***H. Hedenstrom***

study as being best release immediately for fast symptom relief. Taken together with the dosage form of the '448 patent it would have been obvious to treat a bacterial infection with a combination dosage form comprising famotidine and omeprazole. The dosage form would inherently eradicate the infection as evidenced by the ***M. Gschwantler*** study. Barring evidence to the contrary it remain would position of the Examiner that combinations of the prior art would obviate the instant claims.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 571-272-0608. The examiner can normally be reached on M-F 6:00-3:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Micah-Paul Young
Examiner
Art Unit 1618

MP Young

MICHAEL G. HARTLEY
SUPERVISORY [illegible]ER